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EXAMINER	
SASAN, ARADHANA	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/817,335	STANIFORTH ET AL.	
	Examiner	Art Unit	
	ARADHANA SASAN	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 January 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,5,7-12 and 39-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,5,7-12 and 39-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The remarks and amendments filed on 01/12/09 are acknowledged.

2. Claims 1-2, 4-5, 7-12, and 39-52 are included in the prosecution.

MAINTAINED REJECTIONS:

The following is a list of maintained rejections:

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-2, 7-12, 39-40 and 45-50 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Botzolakis et al. (US 4,910,023).

The claimed invention is a method for preparing a tablet, consisting essentially of the steps of: forming an aqueous slurry containing a mixture of microcrystalline cellulose in the form of a wet cake and silicon dioxide having a particle size from about 1 nm to about 100μm; drying the slurry to obtain an excipient comprising a plurality of agglomerated particles of microcrystalline cellulose in intimate association with the silicon dioxide. The amount of silicon dioxide is from about 0.1% to about 20% relative to the amount of microcrystalline cellulose, by weight. Then, a moisture-sensitive active ingredient is mixed with the excipient in a ratio from about 1:99 to about 99:1 to obtain a mixture. The mixture is compressed into a tablet.

Botzolakis teaches that "various unpleasant flavored drugs can be processed by a unique wet granulation process wherein a slurry of the drug in water is dried in combination with colloidal silicon dioxide and, in a particularly preferred embodiment microcrystalline cellulose is used with the colloidal silicon dioxide adsorbing on the drug particles" (Col. 2, lines 11-17). Unpleasant flavored drugs are defined as "drugs which are unpleasant tasting and/or smelling and/or are hygroscopic and/or tacky" (Col. 2, lines 18-21). Examples of hygroscopic or moisture sensitive drugs include "oxtriphylline, procainamide HCl, gemfibrozil, disopyramide phosphate, fenoprofen calcium, atenolol, piracetam, rifamprin, clindamycin HCl, cefaclor, cefadroxil, cephrabine, ascorbic acid, acetysalicylic acid, methocarbamol, methyldopa, ranitine HCl, ethionamide, divalproex sodium, meprobamate, captopril, and aminophylline" (Col. 1, lines 14-25). The drug is present at a level of 30 to 70% by weight (Col. 2, lines 43-44). Example 1 comprises the hygroscopic active phenoxypyridine monosulfate, colloidal silicon dioxide and microcrystalline cellulose (Col. 3, lines 20-55). The drug is milled with colloidal silicon dioxide. An aqueous mixture of sodium lauryl sulfate and water is mixed with the combination of silicon dioxide and the drug. Crospovidone is then added to aid in disintegration. Colloidal silicon dioxide is then added and mixed for about 5 minutes followed by the addition of microcrystalline cellulose. The granulation is then dried in an oven at 50ºC to a moisture content of less than 0.5% and further processed by milling through a 1B screen and then combined with calcium stearate, crospovidone and talc. Tablets are formed by compressing 1140 mg of the mixture to a hardness generally between 18 and 20 Kgm.

Botzolakis does not expressly teach drying a slurry of microcrystalline cellulose and silicon dioxide before mixing with a moisture-sensitive active ingredient.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of making a tablet comprising drying a slurry containing a moisture sensitive active ingredient, colloidal silicon dioxide and microcrystalline cellulose, as suggested by Botzolakis, vary the addition of a moisture sensitive active ingredient to the slurry containing colloidal silicon dioxide and microcrystalline during the process of routine optimization, and produce the instant invention.

One of ordinary skill in the art would do this because during the process of routine experimentation the step of drying the microcrystalline cellulose and colloidal silicon dioxide in the drug slurry can be varied to adding the drug to the dried microcrystalline cellulose and colloidal silicon dioxide slurry. One with ordinary skill in the art would change the addition of drug to the dried microcrystalline cellulose and silicon dioxide mixture in order to optimize the taste masking and desired release profile of the drug. Botzolakis teaches that "a protective coating of silicon dioxide ... masks unpleasant taste and odor and also reduces the adhesive of the granulation onto the punch faces used in the manufacture of the granules. By adsorbing silicon dioxide on the particulate surface of the malflavored hygroscopic drug, the drug becomes not only easier to handle but the unpleasant tastes and/or odors are masked making the final product more susceptible to proper patient compliance" (Abstract).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Regarding instant claims 1 and 39, the limitation of a method for preparing a tablet would have been obvious over the method of preparing a tablet as taught by Botzolakis (Col. 3, lines 20-55). The limitation of forming an aqueous slurry containing a mixture of microcrystalline cellulose in the form of a wet cake and silicon dioxide would have been obvious over the aqueous mixture of sodium lauryl sulfate and water that is mixed with the combination of silicon dioxide and the drug, that is followed by the addition of microcrystalline cellulose (Col. 3, lines 20-55). One with ordinary skill in the art would change the addition of drug to the dried microcrystalline cellulose and silicon dioxide mixture in order to optimize the taste masking and desired release profile of the drug. Botzolakis teaches that "a protective coating of silicon dioxide ... masks unpleasant taste and odor and also reduces the adhesive of the granulation onto the punch faces used in the manufacture of the granules. By adsorbing silicon dioxide on the particulate surface of the malflavored hygroscopic drug, the drug becomes not only easier to handle but the unpleasant tastes and/or odors are masked making the final product more susceptible to proper patient compliance" (Abstract). The particle size of silicon dioxide is a manipulatable parameter that can be modified during the process of routine experimentation in order to achieve the desired dosage, release, stability and

taste profile of the tablet. The limitation of the ratio of moisture sensitive active ingredient to the excipient (about 1:99 to about 99:1) would have been obvious over the drug that is present at a level of 30 to 70% by weight, as taught by Botzolakis (Col. 2, lines 43-44). The limitation of compressing the mixture into a tablet would have been obvious over the compression taught by Botzolakis (Col. 3, lines 51-53).

Regarding instant claims 2 and 40, the limitations of colloidal silicon dioxide and wet granulation prior to compression would have been obvious over the colloidal silicon dioxide (Col. 3, Table 1, lines 25 and 29) and wet granulation prior to compression, as taught by Botzolakis (Col. 3, lines 39-52).

Regarding instant claims 7 and 45, the limitation of adding a further amount of the excipient to the wet granulated mixture would have been obvious over the wet granulation method taught by Botzolakis (Col. 3, lines 39-52). One with ordinary skill in the art would find it obvious to further add the microcrystalline cellulose and silicon dioxide in order to improve flowability and compressibility.

Regarding instant claims 8-12 and 46-50, the limitation of drying the slurry to so that the resultant excipient particles have a moisture content of from about 0.5 to about 15% would have been obvious over the drying that leads to a moisture content of less than 0.5%, as taught by Botzolakis (Col. 3, lines 46-47). One with ordinary skill in the art would find it obvious to modify the drying temperature during the process of routine experimentation in order to optimize the desired moisture content.

5. Claims 4-5, 41-44 and 51-52 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Botzolakis et al. (US 4,910,023) in view of Schmidt et al. (US 4,605,666).

The teaching of Botzolakis is stated above.

Botzolakis does not expressly teach spray drying.

Schmidt teaches a "process for preparing a powder ... which is directly compressible into a tablet prepared by spray drying (a) an aqueous slurry of a water-soluble vitamin and a binder; (b) ... an adsorbent; and (c) a lubricant" (Abstract). It is taught that "the powders are directly compressible into tablets and will not demix" (Abstract). In example 1 an aqueous slurry of ascorbic acid, microcrystalline cellulose and water is spray dried and silicon dioxide is added (Col. 3, lines 29-49). The adsorbent is silicon dioxide (Col. 7, lines 14-15) and the binder is microcrystalline cellulose (Col. 8, lines 4-5).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of making a tablet comprising drying a slurry containing a moisture sensitive active ingredient, colloidal silicon dioxide and microcrystalline cellulose, as suggested by Botzolakis, vary the addition of a moisture sensitive active ingredient to the slurry containing colloidal silicon dioxide and microcrystalline during the process of routine optimization, combine it with the process of spray drying to produce a compressible powder, and produce the instant invention.

One of ordinary skill in the art would do this because spray drying is a method for drying granulations that is known in the art, as evidenced by the teaching of Schmidt.

Regarding instant claim 4, the limitation of spray drying would have been obvious over the spray drying taught by Schmidt (Abstract).

Regarding instant claims 4, 41, 42 and 51, the limitation of the average particle size of about 30μm to about 250μm would have been obvious over the spray drying taught by Schmidt (Abstract) because by manipulating the spray drying process parameters, one with ordinary skill in the art would achieve the recited excipient particle size range unless there is evidence of criticality or unexpected results.

Regarding instant claims 5, 43, 44 and 52, the limitation of the bulk density of the excipient particles from about 0.2g/ml to about 0.6g/ml would have been obvious over the spray drying taught by Schmidt (Abstract) because by manipulating the spray drying process parameters, one with ordinary skill in the art would achieve the recited bulk density range unless there is evidence of criticality or unexpected results.

Double Patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1, 2, 4-5, 7-12, and 51-52 remain rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 20, 21, 23-27 of U.S. Patent No. 6,103,219. Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claims 1, 2, 4-5, 7-12, and 51-52 are drawn to a method for preparing a tablet comprising: forming an aqueous slurry containing a mixture of microcrystalline cellulose in the form of a wet cake and silicon dioxide having a particle size from about 1 nm to about 100 μm; drying said slurry to obtain an excipient comprising a plurality of agglomerated particles of microcrystalline cellulose in intimate association with said silicon dioxide, the amount of silicon dioxide being from about 0.1% to about 20% relative to the amount of microcrystalline cellulose, by weight; mixing an active ingredient with said excipient in a ratio from about 1:99 to about 99:1 to obtain a mixture; compressing said mixture into a tablet.

Claims 20, 21, 23-27 of U.S. Patent No. 6,103,219 ('219) are drawn to a method of preparing a solid dosage form comprising steps identical to those listed above from the instant application. One of ordinary skill in the art would recognize that the method

of preparing a solid dosage form taught in '219, also includes tablets. The claimed subject matter of the instant application is taught by '219. Forming an aqueous slurry containing a mixture of microcrystalline cellulose in the form of a wet cake and silicon dioxide having a particle size from about 1 nm to about 100 μm; drying said slurry to obtain an excipient comprising a plurality of agglomerated particles of microcrystalline cellulose in intimate association with said silicon dioxide, the amount of silicon dioxide being from about 0.1% to about 20% relative to the amount of microcrystalline cellulose, by weight; mixing an active ingredient with said excipient in a ratio from about 1:99 to about 99:1 to obtain a mixture; and incorporating said mixture into a plurality of solid unit doses.

Claim 2 of the instant application is anticipated by claim 21 of '219.

Claim 4 of the instant application is anticipated by claim 24 of '219.

Claim 5 of the instant application is anticipated by claim 25 of '219.

Claim 7 of the instant application is anticipated by claim 27 of '219.

Claims 8-12 of the instant application are drawn to a method of further drying the aqueous slurry so the moisture content of the excipient particles can be controlled. Since the technique of spray drying is used and it is well known in the art, varying the parameters of the spray drying procedure could modify the moisture content of the excipient particles.

Claim 51 of the instant application is anticipated by claim 23 of '219.

Claim 52 of the instant application is anticipated by claim 26 of '219.

Therefore, the claimed subject matter, i.e. a method for preparing a tablet by mixing an active ingredient with the excipient (prepared after forming a slurry containing a mixture microcrystalline cellulose and silicon dioxide, and drying the slurry to get agglomerated particles of microcrystalline cellulose in intimate association with silicon dioxide) and compressing the mixture into a tablet, are anticipated by '219.

8. Claims 39-42, and 46-50 remain rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 19, 20, 24, 30, 32, and 33 of U.S. Patent No. 6,746,693 in view of claims 25-27 of U.S. Patent No. 6,103,219. Although the conflicting claims are not identical, they are not patentably distinct from each other.

Instant claims are drawn to a method for preparing a tablet, comprising the steps of: (a) forming an aqueous slurry of microcrystalline cellulose in the form of wet cake; (b) forming an aqueous slurry of silicon dioxide having a particle size of from about 1 to about 100μm; (c) separately introducing said microcrystalline slurry and said silicon dioxide slurry separately into a drying apparatus for combination therein, to obtain an excipient comprising a plurality of agglomerated particles of microcrystalline cellulose in intimate association with said silicon dioxide, the amount of silicon dioxide being from about 0. 1% to about 20% relative to the amount of microcrystalline cellulose, by weight; (d) mixing an active ingredient with said excipient in a ratio of from about 1:99 to about 99:1 to obtain a mixture; (e) compressing said mixture into a tablet.

Claims 19, 20, 24, 30, 32, and 33 of U.S. Patent No. 6,746,693 ('693) are drawn to a method of preparing a solid dosage form comprising steps identical to those listed

above from the instant application. One of ordinary skill in the art would recognize that the method of preparing a solid dosage form taught in '693, also includes tablets. The claimed subject matter of the instant application is taught by '693. Forming separate aqueous slurries of microcrystalline cellulose and silicon dioxide and introducing these slurries separately into a drying apparatus to obtain an excipient comprising a plurality of agglomerated particles of microcrystalline cellulose in intimate association with the silicon dioxide, the amount of silicon dioxide being from about 0.1% to about 20% relative to the amount of microcrystalline cellulose, mixing an active ingredient with the agglomerated particles, and incorporating the mixture into a plurality of solid unit doses.

Claim 39 of the instant application includes a ratio of active ingredient and excipient of 1:99 to about 99:1. Claim 19 of '693 does not teach this ratio. However, in US 6,103,219 ('219), claim 20 teaches mixing an active ingredient with an excipient in a ratio from about 1:99 to about 99:1. It would have been obvious to one having ordinary skill in the art at the time the invention was made to combine the teaching of '693 (which includes using separate slurries of microcrystalline cellulose and silicon dioxide) with the ratio of active ingredient to excipient taught by '219.

Claim 40 of the instant application is anticipated by claims 20 (further comprises wet granulating the mixture before incorporating into solid unit doses) and 24 (colloidal silicon dioxide) of '693.

Claim 41 of the instant application is anticipated by claim 30 (particle size from 10μm to 1000μm) and claim 37 (spray drying) of '693.

Claim 42 of the instant application is anticipated by claim 32 of '693.

Claims 46-50 of the instant application are anticipated by claim 33 of '693 (which teaches that the moisture content of the particles is from 0.5-15%). Claims 47, 48, 49, and 50 are covered by the range 0.5-15% of the moisture content.

Therefore, the claimed subject matter, i.e. a method for preparing a tablet by mixing an active ingredient with the excipient (prepared after forming separate slurries of microcrystalline cellulose and silicon dioxide and drying the slurry to get agglomerated particles of microcrystalline cellulose in intimate association with silicon dioxide) and compressing the mixture into a tablet, are anticipated by '693.

Response to Arguments

Obviousness-type Double Patenting Rejection

9. Applicants filed new terminal disclaimers properly referencing the instant application number and citing both U.S. Patent Nos. 6,103,219 and 6,746,693 (01/12/09). However, the terminal disclaimers were not approved. Until the terminal disclaimers are approved, the obviousness-type double patenting rejection will be maintained.

Rejection of claims 1-2, 7-12, 39-40 and 45-50 under 35 USC § 103(a)

10. Applicants' arguments, see Page 7, filed 01/12/09, with respect to the rejection of claims 1-2, 7-12, 39-40 and 45-50 under 35 USC § 103(a) as being unpatentable over Botzolakis et al. (US 4,910,023) have been fully considered but are not persuasive.

Applicants argue that the examiner's proposed modification of Botzolakis is incorrect and unsupportable and that one of skill in the art would not change the Botzolakis process by adding the drug to the dried microcrystalline cellulose and silicon

dioxide mixture of the presently claimed invention in order to optimize taste making as the Examiner has asserted. Applicants argue that this modification would not result in the required protective coating of colloidal silicon dioxide onto the maltasting drug particles to provide taste masking of a maltasting drug. Applicants argue that "the Examiner has taken the position, without any supportive evidence whatsoever, that one would modify Botzolakis by coating not the drug, but rather the filler or drying adjunct, to optimize taste masking. Since there is no supportive evidence cited by the Examiner that agglomerated microcrystalline cellulose/colloidal silicon dioxide would provide taste masking of a drug, let alone optimize taste masking, the Examiner's rejection cannot stand. In fact, it appears that the Examiner has chosen an unsuitable motivation, and followed that with a hypothetical, unproven and apparently incorrect conclusion".

Applicants argue that Botzolakis requires that the colloidal silicon dioxide be available to be adsorbed onto the maltasting drug particles creating a protective coating for taste-masking and that Botzolakis describes formulations where microcrystalline cellulose is not in intimate association with colloidal silicon dioxide. Applicants argue that the Examiner's basis for this modification is faulty and unsupportable.

Applicants argue that "Botzolakis fails to provide a basis for a person having ordinary skill in the art at the time of the invention to form a "pre-manufactured" excipient comprising agglomerated particles of microcrystalline cellulose in intimate association with the silicon dioxide, prior to the addition of a moisture-sensitive active agent, which advantageously protects the moisture- sensitive active, as provided by the subject invention. Instead, Botzolakis teaches adding the drug to water in Example 1

and dissolving the drug in water in Example 2. These processes, required to create the taste masking coatings in Botzolakis, are directly contrary to the goal of protecting the moisture-sensitive active agent in the present invention".

Applicants argue that the Examiner's proposed modification would render the prior art unsatisfactory for its intended purpose.

Regarding the obviousness rejections of claims 2 and 40, Applicants argue that the Botzolakis process does not form a "pre-manufactured" excipient comprising agglomerated particles of microcrystalline cellulose in intimate association with the silicon dioxide, prior to the addition of a moisture sensitive active agent.

This is not persuasive because Botzolakis teaches that in a particularly preferred embodiment microcrystalline cellulose with the colloidal silicon dioxide absorbs onto the drug particles (Abstract and Col. 2, lines 11-17). Therefore, the intimate association of the microcrystalline cellulose and silicon dioxide is implicit. Since Botzolakis teaches that microcrystalline cellulose and silicon dioxide are adsorbed onto the drug particles, one of ordinary skill in the art would prepare a mixture of these two components. In order to effectively adsorb the mixture of microcrystalline cellulose and silicon dioxide onto the drug particles, one of ordinary skill in the art would use a slurry of these two components to apply onto the drug particles. The reasoning behind the modification of the process steps of Botzolakis is that during the process of routine experimentation, one of ordinary skill in the art would find it obvious to alter the addition of drug to the slurry comprising a mixture of microcrystalline cellulose and silicon dioxide. The addition of the drug to a dried, pre-formed mixture of microcrystalline cellulose and silicon

dioxide would have been an obvious variant because one of ordinary skill in the art would find it obvious to compare the results of the taste masking of the maltasting drug as it was: a) processed with (i.e., mixed with) a slurry of microcrystalline cellulose and silicon dioxide and then dried; and b) processed with (i.e., mixed with) a dried (pre-formed) mixture of microcrystalline cellulose and silicon dioxide. One of ordinary skill in the art would do this in order to optimize the taste masking of the maltasting drug and determine which process (a) or (b) resulted in superior taste masking. The alteration of the addition steps would have been obvious to one of ordinary skill in the art.

Therefore, the rejection of 07/09/08 is maintained.

Rejection of claims 4-5, 41-44 and 51-52 under 35 USC § 103(a)

11. Applicants' arguments, see Page 12, filed 01/12/09, with respect to the rejection of claims 4-5, 41-44 and 51-52 under 35 USC § 103(a) as being unpatentable over Botzolakis et al. (US 4,910,023) in view of Schmidt et al. (US 4,605,666) have been fully considered but are not persuasive.

Applicants argue that: "the Examiner has relied on a combination of Botzolakis and Schmidt in a further modified, unsupportable manner to create a new invention of her own design. It is respectfully submitted that the modifications that the Examiner suggests be done in order to combine these references in any meaningful way is simply a fabrication which is not supportable by any factual basis. The Examiner's proposed (combined) process would ignore required steps by Botzolakis making an agglomerate of drug/colloidal silicon dioxide; then adding a new step (varying the addition of another ingredient) not taught in either reference; then modifying a spray drying step described

in Schmidt to produce the invention. The Examiner's recreation does not render the claims in question obvious, but rather is an example of an improper use of hindsight based solely on information provided in Applicants' claims". Applicants argue that both Botzolakis and Schmidt fail to teach or suggest dry agglomerated particles of microcrystalline cellulose in intimate association with silicon dioxide as recited in the instant claims.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

In this case, the intimate association of the microcrystalline cellulose and silicon dioxide is implicit, based on a particularly preferred embodiment microcrystalline cellulose with the colloidal silicon dioxide absorbs onto the drug particles, as taught by Botzolakis (Abstract and Col. 2, lines 11-17). The reasoning behind the modification of the process steps of Botzolakis is stated above. During the process of routine experimentation, one of ordinary skill in the art would find it obvious to compare the results of the taste masking of the maltasting drug as it was: a) processed with (i.e., mixed with) a slurry of microcrystalline cellulose and silicon dioxide and then dried; and

b) processed with (i.e., mixed with) a dried (pre-formed) mixture of microcrystalline cellulose and silicon dioxide. One of ordinary skill in the art would do this in order to optimize the taste masking of the maltasting drug and determine which process (a) or (b) resulted in superior taste masking. The alteration of the addition steps would have been obvious to one of ordinary skill in the art. The reasoning behind the combination of Botzolakis and Schmidt is that both references teach granulations of active ingredients. Since spray drying is a known method for drying granulations, as evidenced by Schmidt, one of ordinary skill in the art would find it obvious to try this method for drying the granulation of active ingredient, microcrystalline cellulose and silicon dioxide.

Therefore, the rejection of 07/09/08 is maintained.

Conclusion

12. No claims are allowed.

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Aradhana Sasan/
Examiner, Art Unit 1615

/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615